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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/065,856

11/26/2002

Ann E. Loraine

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06/01/2006

AFFYMETRIX, INC

ATTN: CHIEF IP COUNSEL, LEGAL DEPT.

3420 CENTRAL EXPRESSWAY

SANTA CLARA, CA 95051

EXAMINER

MILLER, MARINA I

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/065,856

Applicant(s)

LORAIN ET AL.

Examiner

Marina Miller

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/6/2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 11-21, 24, 25, 28-37, 40, 41 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 11-21, 24, 25, 28-37, 40, 41 and 43-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/06/2006 has been entered.

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are pending. Claims 6, 8-10, 22-23, 26-27, 38-39, and 42 are cancelled. Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claims 1, 3, 28, and 43, as amended, recite “determining ... splice variants by iteratively fitting the intensity values to a plurality of models of known genomic structure ... wherein the fit of ... models to the intensity values indicates the presence of the alternative splice variants.” However, determining splice variants by iteratively fitting the intensity values to models of known genomic structure wherein the fit of the models to the intensity indicates the presence of the alternative splice variants, does not have support in the specification, claims, or drawings, as originally filed. Specifically, the originally filed specification discloses fitting of “the probe set identifiers and associated hybridization data to models of known genomic structure of alternative splice variants using ... an iterative model-fitting algorithm.” [0119]. The original specification further discloses verifying “a fit of the probe set identifier and hybridization intensity data to a model of a particular splice variant by comparing known function of that splice variant to the collected properties.” [0120]. Applicants amended the specification following paragraph [0120] to introduce the material from application 60/398,958, which is incorporated by reference, disclosing the iterative model fitting. Application 60/398,958 discloses a method for providing relative concentration of splice variants comprising steps of inputting the hybridization intensity and gene structure information, subjecting the input data to model fitting, and deriving relative concentration of splice variants and probe affinity terms (page 4, lines 9-13). Application 60/398,958 further discloses that “the relative transcript concentration can be elucidated by inputting hybridization intensity and gene structure information. ... [A] process of outputting relative transcript concentration by inputting gene structure information and hybridization intensity data through model fitting. Once the relative concentration is calculated, a gene expression profile can be constructed.” (page 10, lines 7-11). Application 60/398,958 also

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discloses that “[t]he model took the gene structure and probe intensities as input data, and output the relative concentration of each variant and the affinity term of each probe” (page 15, lines 3-5). Nowhere does the originally filed application disclose iterative fitting of ONLY intensity (verses intensity **and** gene structure data OR intensity **and** probe set identifier data) to a model of known genomic structure. For these reasons, the claims are rejected for reciting new matter.

Enablement

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7, 11-21, 24-25, 28-37, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims were rejected in the office action mailed 10/06/2005 because the specification does not provide guidance for fitting probe set identifiers and intensity values to a model of genomic structure without knowledge of fitting parameters and/or criteria. The specification further does not provide guidance for how to fit (*e.g.*, statistically, physically, *etc.*), what to fit (*i.e.*, it is not known what probe set identifiers and intensity values represent), and what model to fit (*i.e.*, a genomic structure model is not known). The specification also does not provide any disclosure that the recited “fitting” will determine ASVs.

Applicants amended the specification following paragraph [0120] to introduce the material from application 60/398,958, which is incorporated by reference, disclosing the iterative model fitting. Applicants argue that the amended description includes “an example of a process of fitting hybridization data and models of genomic structure to determine the presence of alternative splice variants” and requested a withdrawal of the enablement rejection (the answer, page 22).

In response, it is noted that application 60/398,958 discloses a linear model that takes a gene structure and probe intensities as input data, and outputs the relative concentration of each variant and the affinity term of each probe (page 15, lines 3-5), wherein each iteration of the algorithm improves the fit of data to a model. The instant specification still does not provide guidance for what to fit (*i.e.*, it is not known what intensity values represent), and what model to fit (*i.e.*, a genomic structure model is not known). Further, the specification does not provide how to fit the intensity to a model without also inputting a gene structure into the model. The specification also does not provide any disclosure that the recited “fitting” will determine ASVs because the model fitting disclosed in application 60/398,958 only yields the relative concentration of known variants and the relative affinity of probes (page 13).

For the reasons stated above and in the previous office action, the examiner maintains that the instant claims are not enabling, and also maintains the rejection.

Second Paragraph

Claims 1-5, 7, 11-21, 24-25, 28-37, and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 43 were previously rejected because the limitation “intensity values detected from each probe-set” was not clear. Applicants amended the claims and argue that the specification describes that “intensity values” of a probe represent a signal measured by a scanner for that probe in a set. In response, it is noted that it is still unclear whether each probe-set is characterized by a total intensity value, or each probe in a probe-set has its own intensity value. It is also unclear whether probe set identifiers identify probe-sets comprising probes and intensities values detected from the probes of probe sets OR whether probe set identifiers identify probe-sets, wherein a probe set comprises probes and intensities detected from the probes. Thus, the examiner maintains that claims 1-2 and 43-45 are indefinite, and also maintains the rejection.

Claims 1, 3, 28, and 43 were rejected because the limitation “fitting ... to models of known genomic structure” was not clear. Applicants amended the specification and the claims and argue that “fitting” is described in the specification. Applicants further argue that one of ordinary skill in the art would understand the limitation “fitting the intensity to a model of known genomic structure “ in light of the amendments to the specification. In response, it is noted that paragraphs [0119]-[0120] cited by applicants, do not disclose what “fitting” is intended, *e.g.*, structural or statistical. Application 60/398,958 discloses linier model fitting that takes a gene structure and probe intensities as input data, and outputs the relative concentration of each

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variant and the affinity term of each probe (page 15, lines 3-5). Neither the claims nor the amended specification defines what “a model of genomic structure” is intended to represent, *e.g.*, a sequence, 3D structure, haplotypes, haplotype blocks, chromosomes, alleles, *etc.* Thus, the examiner maintains that claims 1-5, 7, 11-21, 24-25, 28-37, and 43-45 are indefinite, and also maintains the rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran

5/24/06

Marina Miller
Examiner
Art Unit 1631

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